36. (New) A method for detecting the presence of a mutant $Fkh^{sf}$ polypeptide in a biological sample comprising the steps of:

(a) contacting the biological sample with an antibody, or an antibody fragment thereof, that specifically binds to a mutant $Fkh^{sf}$ polypeptide encoded by a polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1, said region comprising the complement of the sequence set forth in SEQ ID NO:12, under conditions that allow binding of the antibody or antibody fragment to the mutant $Fkh^{sf}$ polypeptide, and

(b) detecting binding of the antibody, or antibody fragment thereof, to the mutant $Fkh^{sf}$ polypeptide.

## REMARKS

Reconsideration of the present Application in view of the present amendments and the following Remarks is respectfully requested. Claims 20-23 are currently pending. Claims 20-23 have been amended and new claims 35-36 have been added to more clearly define the subject matter encompassed by Applicants' invention. Support for the amended and new claims may be found in the specification, for example, at page 3, lines 25-30; page 10, line 26 through page 11, line 8; page 35, lines 20-30; and SEQ ID NOs: 1-4. The Abstract and Title of the application have been amended to more clearly describe the subject matter of the claimed invention in view of Applicants' election of the presently pending claims in response to a Restriction Requirement. The specification has been amended solely to correct typographical errors. The paragraph beginning on line 8 of page 5 was amended to describe the correct length of the nucleotide sequence depicted in Figure 3, and also to describe the correct nucleotide positions that initiate and terminate the coding region. Support for the amended paragraph may be found in the specification at page 34, lines 24-29, and in SEQ ID NO:3. No new subject matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

OBJECTIONS TO THE SPECIFICATION

The Examiner objects to the specification, asserting that the paragraph beginning on page 1, line 5, should be amended to reflect the status of the parent application, Serial Number 09/372,668.

Applicants have submitted herewith an amendment to the specification to reflect cross-references to related applications. Applicants therefore respectfully request that the objection be withdrawn.

The Examiner objects to the Title of the instant Application, asserting that the Title is not descriptive of the invention to which the claims are directed.

Applicants have amended the Title of the present Application in view of Applicants' election of the presently pending claims in response to a Restriction Requirement. Applicants therefore respectfully request that the objection to the Title be withdrawn.

The Examiner objects to the Abstract of the Disclosure, alleging that the Abstract does not adequately describe the claimed invention.

Applicants submit that according to the amendment submitted herewith, the Abstract adequately describes the claimed invention. Applicants therefore respectfully request that the objection to the Abstract be withdrawn.

OBJECTION TO THE DRAWINGS

The PTO objects to the drawings, asserting that the drawings fail to comply with 37 C.F.R. § 1.84. Specifically, the Draftsperson asserts that Figure 6 does not comply with 37 C.F.R. § 1.84(b); that Figure 9 does not comply with 37 C.F.R. § 1.84(g); that Figures 5-10 do not comply with 37 C.F.R. § 1.84(l); and that Figures 1-10 do not comply with 37 C.F.R. § 1.84(p). The Examiner asserts that corrected drawings must be submitted.

Applicants include herewith new, corrected drawings with the present amendment. Applicants respectfully submit that the corrected drawings comply with 37 C.F.R. §§ 1.84(b), (g), (l), and (p) and request that the Examiner withdraw the objection.

INFORMATION DISCLOSURE STATEMENT (IDS)

The Examiner notes that Applicants' amendment filed October 24, 2000, stated that an IDS was filed with the prior application, Serial Number 09/372,668. The PTO, however cannot locate the references, and the Examiner requests that the references be resubmitted.

Applicants are resubmitting herewith the references listed in the IDS as filed in the prior application, Serial Number 09/372,668, as well as a copy of Form PTO-1449 submitted at the time of filing of this application, for the Examiner's review.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The PTO rejects claims 20-23 under 35 U.S.C. § 112, second paragraph, asserting that the claims are indefinite. In particular, the Action asserts that the recitation "Fkh$^{sf}$" is an arbitrary designation that renders the claim indefinite by identifying the gene product without providing a SEQ ID NO.

Applicants respectfully traverse these grounds for rejection and submit that the present specification unambiguously defines an *Fkh$^{sf}$* gene and gene product, such that the recitation "Fkh$^{sf}$" clearly points out and distinctly claims the subject matter of the invention (*e.g.*, page 2, line 25 through page 3, line 4; page 32, line 26 through page 33, line 7). Nevertheless, solely to expedite prosecution of the present Application, Applicants have amended claims 20-23 to recite sequence identifiers of the polypeptide to which the antibodies specifically bind in the claimed method, thus particularly pointing out and distinctly claiming what Applicants regard as their invention. Applicants therefore submit that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection of the claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

The PTO rejects claims 20-23 under 35 U.S.C. § 112, first paragraph, alleging lack of enablement. The PTO concedes that the specification enables a method of detecting the presence of an Fkh$^{sf}$ polypeptide that comprises the amino acid sequence of SEQ ID NO:2 or 4 using an antibody that binds to such a polypeptide. The Action asserts, however, that the specification does not enable an antibody that can detect the presence of any Fkh$^{sf}$ or any mutant

thereof. The Action further alleges that the scope of the claims is not commensurate with the subject matter enabled by the disclosure.

Applicants respectfully traverse these grounds for rejection and submit that as disclosed in the specification and recited in the claims, the claimed invention was fully enabled at the time the Application was filed. Applicants' invention is directed to a method of detecting the presence of an $Fkh^{sf}$ polypeptide in a biological sample, comprising the steps of (a) contacting the biological sample with an antibody, or an antibody fragment thereof, that specifically binds to an $Fkh^{sf}$ polypeptide that comprises the amino acid sequence set forth in SEQ ID NO:2, under conditions that allow binding of the antibody or antibody fragment to the $Fkh^{sf}$ polypeptide; and (b) detecting binding of the antibody, or antibody fragment thereof, to the $Fkh^{sf}$ polypeptide. In another embodiment, the invention is directed to a method for detecting the presence in a biological sample of an $FKH^{sf}$ polypeptide comprising the steps as recited but using an antibody that specifically binds to an $FKH^{sf}$ polypeptide that comprises the amino acid sequence set forth in SEQ ID NO:4.

Applicants respectfully submit that the specification clearly teaches a skilled artisan how to make and use the claimed invention without undue experimentation. As conceded by the PTO, the specification enables a method of detecting the presence of an $Fkh^{sf}$ polypeptide comprising the amino acid sequence of SEQ ID NO:2 or the presence of an $FKH^{sf}$ polypeptide comprising the amino acid sequence of SEQ ID NO:4 using antibodies that bind to such polypeptides. Antibodies that specifically bind to an $Fkh^{sf}$ polypeptide or an $FKH^{sf}$ polypeptide may be generated by methods disclosed in the specification (*e.g.*, page 24, line 10 through page 25, line 30) and known in the art, and may be identified by any number of immunological assays, which are also described in the specification (*e.g.*, page 24, line 29 through page 25, line 11) and known in the art. Furthermore, using the antibodies that specifically bind the novel $Fkh^{sf}$ and $FKH^{sf}$ polypeptides, comprising SEQ ID NOs: 2 and 4, respectively, a person skilled in the art may make and use the claimed method for detecting the presence of such polypeptides in a biological sample according to a variety of immunoassay techniques. These techniques include, for example, countercurrent immunoelectrophoresis, radioimmunoassays, and ELISAs, which may further incorporate a competition or inhibition format (*see, e.g.*, specification, page 11, lines 3-8 and references cited therein).

Applicants therefore respectfully submit that given the teachings of the present specification and the level of skill in the art, generating and identifying antibodies that specifically bind to an $Fkh^{sf}$ polypeptide comprising the amino acid sequence of SEQ ID NO:2 or an $FKH^{sf}$ polypeptide comprising the amino acid sequence of SEQ ID NO:4 for use in the claimed methods would not amount to undue experimentation, but instead is merely a matter of permissible routine screening. (*See In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) ("Enablement is not precluded by the necessity for some experimentation such as routine screening."). Accordingly, Applicants respectfully submit that the present specification satisfies the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants therefore request that the rejection of the claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The PTO rejects claims 20-23 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. The PTO concedes that at the time of filing the priority application, Applicants had possession of a method of detecting the presence of $Fkh^{sf}$ comprising the amino acid sequence of SEQ ID NO:2 or 4 using an antibody that binds to such a polypeptide. However, the Action alleges that Applicants did not have possession of a method of detecting the presence of any $Fkh^{sf}$ polypeptide or any mutant thereof. The Action further asserts that Applicants have not adequately described common structural and functional properties of species within the recited genus of $Fkh^{sf}$ polypeptides.

Applicants respectfully traverse these grounds for rejection and submit that Applicants possessed the claimed invention, as disclosed in the present specification and recited in the instant claims, at the time the application was filed. As the PTO concedes, the instant specification reasonably conveys to a person skilled in the art that Applicants possessed the claimed method of detecting in a biological sample the presence of an $Fkh^{sf}$ polypeptide using an antibody or fragment thereof that specifically binds to an $Fkh^{sf}$ polypeptide comprising the sequence set forth in SEQ ID NO:2, or detecting the presence of an $FKH^{sf}$ polypeptide, using an antibody or fragment thereof that specifically binds to an $FKH^{sf}$ polypeptide comprising the sequence set forth in SEQ ID NO:4. In certain embodiments, the claimed method for detecting

the presence of an $Fkh^{sf}$ polypeptide comprises the use of an antibody, or fragment thereof, that specifically binds a (murine) $Fkh^{sf}$ polypeptide comprising the amino acid sequence as set forth in SEQ ID NO:2, which is encoded by a polynucleotide comprising the sequence set forth in SEQ ID NO:1. In certain other embodiments, the method for detecting the presence of an $FKH^{sf}$ polypeptide comprises the use of an antibody, or a fragment thereof, that specifically binds to a (human) $FKH^{sf}$ polypeptide comprising the amino acid sequence as set forth in SEQ ID NO:4, and which is encoded by a polynucleotide comprising the sequence set forth in SEQ ID NO:3. Applicants submit that the disclosure of the polynucleotide sequences and the deduced amino acid sequences of the novel $Fkh^{sf}$ and $FKH^{sf}$ polypeptides, provides specific, detailed, and complete chemical formulas enabling a skilled artisan to generate and identify antibodies that specifically bind to such polypeptides for use in the claimed methods.

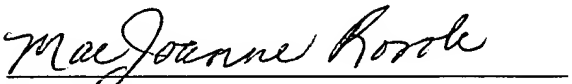
In view of the above remarks and the present amendment, Applicants respectfully submit that the subject matter claimed is sufficiently described by the specification to reasonably convey to a person skilled in the art that Applicants possessed the claimed invention at the time the Application was filed. Applicants therefore submit that the instant Application complies with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of the claims be withdrawn.

All claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Mary E. Brunkow et al.

SEED Intellectual Property Law Group PLLC



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Enclosures:

Postcard
11 Sheets of Drawings (Figs. 1A-10)
Copy of Cited References (13)
Copy of Form PTO-1449

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Abstract:

The Abstract has been amended as follows:

Isolated nucleic acid molecules are provided which encode $Fkh^{sf}$, as well as mutant forms thereof. Also provided are expression vectors suitable for expressing such nucleic acid molecules, and host cells containing such expression vectors. ~~Utilizing assays~~ Assays that are based upon the nucleic acid sequences disclosed herein (as well as mutant forms thereof), may be used for identifying numerous molecules ~~may be identified which~~that modulate the immune system. Molecules that specifically bind to an $Fkh^{sf}$ polypeptide are also provided as useful, such as, for modulating the biological activities of $Fkh^{sf}$. In particular, antibodies that are specific for an $Fkh^{sf}$ polypeptide are provided that may be used in methods such as for detecting an $Fkh^{sf}$ polypeptide, isolating an $Fkh^{sf}$ polypeptide, and modulating the activity of an $Fkh^{sf}$ polypeptide.

In the Specification:

The Title of the application has been amended as follows:

~~Identification of~~Methods for Detecting a ~~the~~ Wild-Type $Fkh^{sf}$ Gene Product and Its Human Ortholog and for Detecting a Mutant $Fkh^{sf}$ Gene Product Causing the Mouse Scurfy Phenotype ~~and Its Human Ortholog~~

The paragraph beginning at line 4 of page 1 has been amended as follows:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional of United States Patent Application No. 09/372,668, filed August 11, 1999, now issued U.S. Patent No. 6,414,129, which claims ~~priority from~~ the benefit of U.S. Provisional Application No. 60/096,195, filed August 11, 1998~~,~~. ~~which~~ The contents of all the above applications ~~is~~ are incorporated herein by reference in ~~its~~ their entirety.

The paragraph beginning at line 4 of page 5 has been amended as follows:

Figure 1 depicts a nucleotide sequence of mouse *Fkh*$^{sf}$ cDNA (~~Seqeunce~~ Sequence I.D. No. 1); translation is predicted to initiate at position 259 and terminate at position 1546.

The paragraph beginning at line 9 of page 5 has been amended as follows:

Figure 3 depicts a nucleotide sequence of ~~1735~~ 1869 bp corresponding to human *FKHsf* cDNA (Sequence I.D. No. 3; including a 1293 bp coding region); translation is predicted to initiate at position ~~55~~ 189 and terminate at position ~~1348~~1482.

The paragraph beginning at page 24, line 10 has been amended as follows:

Antibodies which modulate the immune system may readily be prepared given the disclosure provided herein. Within the context of the present invention, antibodies are understood to include monoclonal antibodies, polyclonal antibodies, anti-idiotypic antibodies, antibody fragments (*e.g.*, Fab, and $F(ab')_2$, $F_V$ variable regions, or complementarity determining regions). As discussed above, antibodies are understood to be specific against Fkh$^{sf}$ if they bind with a $K_a$ of greater than or equal to $10^7$-$M^{-1}$, preferably greater than of equal to $10^8$-$M^{-1}$. The affinity of a monoclonal antibody or binding partner, as well as inhibition of binding, can be readily determined by one of ordinary skill in the art (*see* Scatchard, *Ann. N.Y. Acad. Sci. 51*:660-672, 1949).

The paragraph beginning at line 24 of page 34 has been amended as follows:

Figure ~~4~~ 3 shows the nucleotide sequence of the 1869 bp cDNA obtained to date (including an 1293 bp coding region); translation is predicted to initiate at position 189 and terminate at position 1482. Figure 4 shows the sequence of the 431 amino acid human FKH$^{sf}$ protein. Comparison of the predicted coding region of the human gene to the mouse cDNA sequence reveals nearly identical exon structure and 86.1% amino acid sequence identity across the entire protein.

In the Claims:

Claims 20 and 21 have been amended and new claims 35-36 have been added as follows:

20. (Amended) A method of detecting the presence of an $Fkh^{sf}$~~, or a mutant form thereof,~~ polypeptide in a biological sample, comprising the steps of:

(a) contacting said biological sample with an antibody, or an antibody fragment thereof, ~~anti-~~that specifically binds to an $Fkh^{sf}$ polypeptide that comprises the amino acid sequence set forth in SEQ ID NO:2, ~~antibody or an antibody fragment, wherein said contacting is performed~~ under conditions that allow ~~the~~ binding of said antibody or antibody fragment to ~~said~~the ~~biological sample~~ $Fkh^{sf}$ polypeptide~~,~~; and

(b) detecting ~~any of said bound~~binding of the antibody, or ~~bound~~ antibody fragment thereof, to the $Fkh^{sf}$ polypeptide.

21. (Amended) The method of any one of claims 20, 35-36 wherein said antibody ~~or said antibody fragment~~ is selected from the group consisting of:

(a) polyclonal antibody,

(b) a murine monoclonal antibody,

(c) a humanized antibody derived from (b),

(d) a human monoclonal antibody, and

~~(e) an antibody fragment derived from (b), (c) or (d).~~

22. (Amended) The method of any one of claims 20, 35-36, wherein said antibody fragment is selected from the group consisting of $F(ab')_2$, $F(ab)_2$, Fab', Fab, Fv, sFv, and minimal recognition unit.

23. (Amended) The method of any one of claims 20, 35-36, wherein said antibody or said antibody fragment further comprises a detectable label selected from the group consisting of radioisotope, fluorescent label, chemiluminescent label, enzyme label, bioluminescent label, and colloidal gold.

35. (New) A method for detecting the presence of an $FKH^{sf}$ polypeptide in a biological sample, comprising the steps of:

(a) contacting the biological sample with an antibody, or an antibody fragment thereof, that specifically binds to an $FKH^{sf}$ polypeptide that comprises the amino acid sequence set forth in SEQ ID NO:4, under conditions that allow binding of the antibody or antibody fragment to the $FKH^{sf}$ polypeptide, and

(b) detecting binding of the antibody, or antibody fragment thereof, to the $FKH^{sf}$ polypeptide.

36. (New) A method for detecting the presence of a mutant $Fkh^{sf}$ polypeptide in a biological sample comprising the steps of:

(a) contacting the biological sample with an antibody, or an antibody fragment thereof, that specifically binds to a mutant $Fkh^{sf}$ polypeptide encoded by a polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1, said region comprising the complement of the sequence set forth in SEQ ID NO:12, under conditions that allow binding of the antibody or antibody fragment to the mutant $Fkh^{sf}$ polypeptide, and

(b) detecting binding of the antibody, or antibody fragment thereof, to the mutant $Fkh^{sf}$ polypeptide.

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